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Chemical Basis of Tissue Destruction in Obstructive Lung Disease.

This study is designed to define the role of elastases of alveolar macrophages and of circulating polymorphonuclear leukocytes in the development of pulmonary emphysema in human subjects. Assays of elastase activity will be performed using an oxalate-treated elastin substrate developed in the investigator's laboratory. Leukocytes are obtained by phlebotomy and macrophages will be harvested by bronchoscopic lavage from several patient groups: (1) normal subjects with isolated radiologic lesions requiring bronchoscopy; (2) patients with chronic obstructive lung disease whose physiological and clinical manifestations are primarily those of pulmonary emphysema, and (3) patients with chronic obstructive lung disease with characteristics primarily of bronchitis. Distinctions will also be sought between smokers and nonsmokers. Elastase activity in macrophages from animals with experimental emphysema induced by proteolysis will be assayed also.

The effects of reagents such as cytochalasin, colchicine and thioglycollate on the levels of macrophage elastase activity will be studied in tissue culture of alveolar macrophages. These agents produce marked changes in elastase activity in peritoneal macrophages. Chloromethylketone derivatives which inhibit pancreatic and leukocyte elastase will be studied for inhibition of alveolar macrophage elastase.

The ultimate purpose of these investigations is to evaluate the potential role of alveolar macrophage elastase activity as an etiological agent in tissue destructive changes in airway obstructive diseases of the lung.

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